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### Cognitive consequences of overweight and obesity in the ninth decade of life?

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## **Cognitive Consequences of Overweight and Obesity in the 9<sup>th</sup> decade of life?**

## **Abstract**

**Background/objectives.** The association between late life obesity and late life cognitive abilities is poorly understood. We studied the association between body mass index (BMI) and cognitive change in longitudinal population-based study spanning over the 9<sup>th</sup> decade of life.

**Subjects/Methods.** In total, 475 participants free of dementia at baseline from the Lothian Birth Cohort 1921 (mean age 79.1 years, SD 0.6) were included. Height and weight were assessed at baseline. BMI was calculated as kg/m<sup>2</sup>. Cognitive abilities were assessed at age ~11 years and at age ~79, ~83, ~87, and ~90 years.

**Results.** Latent growth models showed that men being overweight and obese had a 0.65 (SD 0.3) and 1.10 (SD 0.5) points less steep decline in general cognitive ability (as measured by the Moray House Test) for each year than people of normal weight. These associations were to some extent confounded by childhood intelligence. No other association between BMI and cognition was significant, either for men or women. People who were obese in old age had significantly lower childhood intelligence ( $m = 43.6$ , SD 1.3) than people who were normal in weight ( $m = 47.0$ , SD 0.8) and persons being overweight ( $m = 47.5$ , SD 0.8),  $F(472, 3) = 3.2$ ,  $p = .043$ .

**Conclusions.** The current study shows weak or no evidence for an association between BMI in old age and cognitive function, especially not when childhood intelligence is controlled for. Lower intelligence at the age of 11 years predicted obesity at the age of 79 years.

Keywords: Aged; Aged, 80 and over; Body Mass Index; Cognition; Intelligence;  
Longitudinal studies

Key points:

- The current study shows weak or no evidence for an association between BMI in old age and cognitive functioning neither at the mean level or individual level, especially not when intelligence in childhood is controlled for.
- Men being overweight in old age might have a less steep decline in general cognitive ability than men being normal weight.
- Lower intelligence at the age of 11 years predicted obesity at the age of 79 years.

## **Introduction**

There is an ongoing debate in the literature about what should be considered a healthy body mass index (BMI) in late life. Late life BMI has been studied in relation to various outcomes in late life, but the association is poorly understood [1], and not least when it comes to cognitive abilities [2]. Given that maintaining cognitive abilities is among the most important aspects of health and quality of life in old age, an increased understanding of the association between late life BMI and cognitive abilities is of importance for public health.

Current studies have linked both low BMI and high BMI to lower cognitive abilities in later life [3-8]. These findings are mainly based on studies with a cross-sectional design or studies with short-term follow-up. This limits the possibility of evaluating the longer-term associations between BMI and cognitive change, and of finding some indication of the direction of the association. Studies with a longitudinal design can overcome these limitations, by evaluating the association between a trait and individual change; in the present study we examine the association between BMI and cognitive change in old age taking gender differences and early life cognitive ability into account.

## **Methods**

### *Study participants*

Data from the Lothian Birth Cohort 1921 (LBC1921) were used. In 1999, surviving participants of the Scottish Mental Survey 1932 (SMS1932) living in the Edinburgh area were recruited via general practitioners' patient lists and advertisements in the media, as described elsewhere [9, 10]. Between 1999 and 2001, 550 volunteers

participated in an in-person testing session. Among these, six participants had missing information about BMI, and 57 had no traceable childhood intelligence score from the SMS1932. Further, 13 participants had missing data on either some of the cognitive tests or covariates. In total, 475 persons had complete data on all relevant variables at baseline. Since 1999 ( $m = 79.1$  years,  $SD\ 0.6$ ), three additional waves of data have been collected: the second was in 2003-2005 ( $m = 83.3$  years,  $SD\ 0.5$ ), the third was in 2007-2008 ( $m = 86.6$  years,  $SD\ 0.4$ ), and the fourth was in 2011 ( $m = 90.1$  years,  $SD\ 0.1$ ).[11] Cognitive test scores from all four waves of testing were used.

### *Body Mass Index*

Trained research nurses following a standardized protocol assessed height and weight at baseline. Body Mass Index (BMI) was calculated as weight (in kilograms) divided by height (meters) squared. BMI was used both as a continuous and categorized variable. BMI was categorized according to the World Health Organization's recommendations: underweight ( $BMI < 18.5\text{ kg/m}^2$ ), normal weight ( $18.5 \leq BMI < 25\text{ kg/m}^2$ ), overweight ( $25 \leq BMI < 30\text{ kg/m}^2$ ), and obese ( $BMI \geq 30\text{ kg/m}^2$ ).[12] Given that only 7 (1.7 %) persons were considered to be underweight, this category could not be included in analyses using BMI as a categorical variable. Neither did we reach a sufficient number of underweight people (an additional 8 people) when a less restrictive cut-off for underweight was used, *i.e.*  $BMI < 20.0\text{ kg/m}^2$ .

### *Cognitive tests*

Of the cognitive tests included in LBC1921, four tests had been assessed three or four times in late life and showed a significant age-related mean decline. The Moray House Test No. 12 (MHT) assesses general cognitive ability by several types of item,

predominated by verbal reasoning [13]. The MHT was taken at age 11 and at wave1, wave 3 and wave 4 in older age. Raven's Standard Progressive Matrices measures nonverbal reasoning abilities; the participants are asked to select the correct pattern that completes incomplete abstract patterns [14]. This test was available from all four waves. Two additional tests were distributed which started at wave 2: Wechsler Digit Symbol and Letter-Number Sequencing. Digit Symbol measures processing speed. Participants are asked to write down as many symbols corresponding to a given number as fast as possible within two minutes [15]. Letter-Number sequencing is a test of working memory. Participants are asked to remember increasingly long series of jumbled letters and numbers that are read out loud to them. They are asked to repeat them by naming the numbers first in numerical order followed by the letters in alphabetical order [15].

The Mini-Mental State Examination (MMSE)[16] was available across all waves. The MMSE is a screening tool for cognitive impairments, and a score below 25 (out of 30) is often used as an indication of cognitive impairment or as a proxy of dementia [17, 18]. A MMSE score below 25 should be viewed as only a suspicion of dementia, as compared to a diagnosis of dementia, and will be referred to as suspicion of dementia in the current manuscript.

### *Covariates*

The UK standard Classification of Occupations (from the United Kingdom's Office of Population and Census Studies) was used to assess social class where lower scores relate to more professional occupations.[19] People were categorized based on their most professional regular occupation. For women, the highest-rated occupation was

used, taking their own and their husband's occupation into account. Cardiovascular disease and cerebrovascular events were self-reported at baseline and summed into one score. Only 20 persons (4.2%) reported having experienced both a cardiovascular and cerebrovascular event (CVD); hence, instead of using CVD as a continuous variable, CVD was dichotomized as no prevalence of CVD (=0) and prevalence of CVD (=1). Prevalence of diabetes was self-reported at baseline, and scored as no prevalence of diabetes (=0) and prevalence of diabetes (=1).

### **Statistical analyses**

All descriptive analyses were performed in IBM SPSS version 21[20] and all longitudinal analyses in SAS 9.1 [21]. Sex differences were compared with t-tests and Chi-square tests as appropriate. Differences between normal weight, overweight, and obese persons were compared with univariate Analyses of Variance (ANOVA). All continuous variables were normally distributed.

To assess cognitive change latent growth curve modeling with a full maximum-likelihood estimate (MLE) technique was used [22], employing PROC MIXED in SAS. Growth curves were fit to establish linear age trajectories. For the MHT and for Raven's Progressive Matrices, mean-centered age (linear) at 80 years were used, as this is an age where it has been suggested that the age-related cognitive decline is accelerated [23]. For Digit Symbol and Letter-Number Sequencing, the mean age at wave2, 83.3 years, was used, as the centering point, because these tests were not assessed at wave1. No significant evidence for nonlinear age-related change (curvilinear change) was found in any of the models, and therefore only linear change was examined.



A stepwise procedure was adopted to evaluate longitudinal trajectories for each cognitive domain, first including both men and women, and then separately for men and women. The baseline model included linear age, BMI (both continuous and categorical associations were tested), an interaction term between linear age and the BMI variable (to assess difference in cognitive change based on BMI), and baseline age. Given that U-shaped or J-shaped associations between late life-BMI and various traits have previously been reported, both normal weight and overweight were tested as the reference category.

In the second set of models we controlled for: childhood intelligence, social class, CVD, and for suspicion of dementia. Each of these covariates were entered separately and, if the covariate improved the model fit (as evaluated by the -2Log Likelihood Test), it was retained in the model.

## **Results**

Baseline characteristics for the total sample and based on sex are presented in table 1. Mean values and the number of men and women who performed the cognitive tests at each assessment wave are presented in appendix 1.

*Insert table 1 about here*

Participants who were obese in late life had significantly lower childhood intelligence ( $m = 43.6$ ,  $SD 1.3$ ) than those who were normal in weight ( $m = 47.0$ ,  $SD 0.8$ ) and overweight ( $m = 47.5$ ,  $SD 0.8$ ),  $F(472, 3) = 3.2$ ,  $p = .043$ . Participants

who were obese in old age did not differ significantly on the MHT ( $m = 56.9$ , SD 1.2) in old age compared to those who were of normal weight ( $m = 59.0$ , SD 0.8) and overweight ( $m = 59.9$ , SD 0.7),  $F(472, 3) = 2.22$ ,  $p = .110$ . There were no significant differences in cognitive performance at age 79 baseline based on BMI group: Raven's Matrices ( $p = .371$ ), Digit Symbol<sub>wave2</sub> ( $p = .935$ ), Letter-Number Sequencing<sub>wave2</sub> ( $p = .143$ ). There was no significant difference in CVD prevalence at baseline based on BMI category ( $p = .918$ ). Prevalence of diabetes tended to be more common in the obese group (10%) compared to the normal (4.1%) and overweight (3.4%) groups,  $\chi^2(2, N = 475) = 5.85$ ,  $p = .054$ .

Neither continuous BMI nor categorical BMI (independent of which BMI category were used as reference category) were significantly related to either mean level cognitive performance, or to cognitive decline in any test, when men and women were analyzed jointly (data not shown).

The influence of BMI on cognitive abilities separately for men and women are shown in table 2 and figure 1. Overweight and obese men had significantly shallower declines on the MHT than men of normal weight. The effect is clearest in obese people. This effect was also statistically significant when BMI was used as a continuous variable:  $.103$ ,  $p = .017$ . Similar patterns appeared for men in all the cognitive tests, although none of these other test scores reached statistical significance (figure 1). To evaluate whether those with the lowest BMI drove the negative effect of being normal weight on general cognitive ability, we also tested the association when participants with a BMI below 20 kg/m<sup>2</sup> were excluded. This did not change the association. For women, no effect of BMI on

mean level cognitive performance or cognitive change (linear age) was found, as can be seen in table 2.

*Insert table 2 about here*

*Insert figure 1 about here*

The subsequent models were conducted for only men and for only the MHT. In the next step, when MHT at age 11 was added into the model, the estimates for the impact of overweight and obesity on cognitive change decreased from 0.65 to 0.52 ( $p = .056$ ), and from 1.10 to 0.53 ( $p = .196$ ), respectively. Neither social class, CVD, nor diabetes were significantly associated with performance on the MHT, nor did they improve the model fit. When suspicion of dementia was added to the model the estimates for the influence of overweight and obesity changed to .60,  $p = .023$  and .61,  $p = .120$ , respectively.

## **Discussion**

No previous study has focused on the association between BMI and age-related cognitive change among persons in the 9<sup>th</sup> decade of life. One significant finding was that overweight and obese men had a less steep decline in general cognitive ability than men of normal weight. No association between BMI and cognitive function was found among men or women.

However, the association between obesity, and less steep global cognitive decline among men, was confounded by childhood intelligence. This finding should be interpreted with caution, as few men were obese at baseline. It is more relevant

to focus on the fact that the overweight-global cognitive change association was not substantially attenuated by childhood intelligence. This finding adds to the literature that supports the suggestion that the optimal BMI is higher in old age than in middle age.

It is possible that both cognitive decline and low BMI (caused by weight decline) originates from some common pathology. For example, both weight loss and cognitive decline have been associated with the preclinical process and the clinical process of dementia [28, 29]. In this case, being overweight (and sometimes even being obese) might become an indication of cognitive health in late life. Indeed, the association between obesity and less steep cognitive decline attenuated and became non-significant when suspicion of dementia was controlled for, but the protective effect of being overweight on cognitive development remained significant.

Another relevant finding from this study is that lower childhood intelligence at the age of eleven predicted higher BMI at the age of 79 years. This finding extends previous findings that found that low childhood intelligence predicts overweight and/or obesity in middle age [30], and late life [6]. Still, this might seem contradictory to the finding that persons being obese in old age had less cognitive decline compared to people of normal weight. However, it is important to differentiate between analyses on the mean level and the individual level. As can be seen in figure 1, persons who were obese in old age usually had the lowest cognitive abilities at the start of the study (although not statistically significant), but declined less than people of normal weight.

The potential sex difference in the BMI-cognitive change association might originate from the measure of fat mass, as a BMI score does not always correspond to the same degree of fat mass in men and women [24]. It is known that fat and especially abdominal fat (not available in the current study) is associated with an increased risk of CVD, and is one of the main explanations why men have a higher incidence of CVD than women. No measure of fat mass other than BMI was available. However, it was possible to evaluate whether CVD modified the BMI-cognitive change association among men, which it did not. We can only speculate about other potential causal pathways. For example, hormones produced and/or secreted from the adipocytes such as testosterone, estradiol, and leptin have been proposed to be related to cognitive functioning [25, 26]. Another possible explanation of the sex difference is that women's weight fluctuates more than men's [27], and so a single measure of fat mass might be a less good indicator of health for women than for men in old age.

Strengths of this study include the longitudinal design with up to four measures of cognitive abilities over an eleven-year period covering the whole of the 9<sup>th</sup> decade of life, the narrow age range of the participants, and the availability of cognitive ability data from childhood. Although the sample size was relatively large at baseline, especially given that it is a study with focus on people in the 9<sup>th</sup> decade of life, the sample becomes much smaller at the latter assessment waves. Hence, there is the possibility that the significant finding is a type 1 error, and it would not survive Bonferroni-type correction. Therefore, the finding requires replication.

There might also have been a selection bias of healthier individuals and individuals less affected by the potential negative effects of being overweight and obese in old age (survival bias), as in all studies including older adults. It is a limitation that BMI or no other anthropometric measures was not available from early life or assessed at the second wave of the study, so we were not able to evaluate either long-term or short-term changes in BMI in relation to cognitive decline, or other measures of fat mass.

The current study shows weak or no evidence for an association between BMI in old age and cognitive function, especially not when childhood intelligence is controlled for. Lower intelligence at the age of 11 years predicted obesity at the age of 79 years.

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**Table 1.** Sample Characteristics at Baseline, Total Sample, and by Sex.

	Total	Men	Women	<i>P</i> - value
	n = 475	n = 200	n = 275	
Age, mean (SD)	79.1 (0.6)	79.1 (0.6)	79.1 (0.6)	0.753
BMI at baseline, mean (SD)	26.3 (4.0)	26.3 (3.5)	26.3 (4.3)	0.970
Normal weight, n (%)	194 (40.6)	76 (38.0)	117 (42.6)	
Overweight, n (%)	203 (42.7)	96 (48.0)	107 (38.9)	
Obese, n (%)	79 (16.6)	28 (14.0)	51 (18.5)	0.118
Moray House Test, mean (SD)	59.0 (10.6)	59.9 (10.6)	58.4 (10.7)	0.123
Raven's Matrices, mean (SD)	30.9 (8.7)	32.3 (8.7)	30.9 (8.6)	0.005
Digit Symbol, mean (SD), n=289 <sup>a</sup>	41.3 (12.6)	41.7 (11.8)	41.0 (13.2)	0.632
Letter-Number Seq., mean (SD), n=290 <sup>a</sup>	9.6 (2.8)	9.6 (2.6)	9.7 (2.9)	0.833
Moray House Test <sub>age 11</sub> , mean (SD)	46.7 (11.9)	46.1 (12.7)	47.1 (11.3)	0.371
Social class I, (n, %)	107 (22.6)	54 (27.0)	53 (19.3)	

Social class II, (n, %)	156 (32.9)	66 (33.0)	90 (32.9)	
Social class III-V, (n, %)	211 (44.5)	80 (40.0)	132 (47.8)	0.102
CVD, n (%)	167 (35.2)	89 (44.5)	78 (28.4)	<0.001
Diabetes, n (%)	23 (4.8)	11 (5.5)	12 (4.4)	0.571

<sup>a</sup> Digit Symbol and Letter-Number Sequencing were not available at the first assessment wave, therefore these numbers are based on data from the second wave of data collection.



**Table 2.** Associations between Old-old Age BMI (Age 80) and Cognitive Mean Level Test Performance and Longitudinal Trajectories of Change in Old-old Age. <sup>a</sup>

		Moray' House Test			Raven's Matrices			Digit Symbol			Letter-Number Sequencing		
Effect	BMI Group	Estimate	SE	P-value	Estimate	SE	P-value	Estimate	SE	P-value	Estimate	SE	P-value
<u>Men</u>													
Intercept <sub>80/83</sub> <sup>b</sup>	Normal (Ref)	<b>60.9</b>	<b>1.7</b>	<b>&lt;.001</b>	<b>32.3</b>	<b>1.1</b>	<b>&lt;.001</b>	<b>49.4</b>	<b>3.3</b>	<b>&lt;.001</b>	<b>9.87</b>	<b>0.7</b>	<b>&lt;.001</b>
	Overweight <sup>c</sup>	0.55	1.7	.742	-0.86	1.1	.436	-5.32	3.7	.157	-0.34	0.8	.685
	Obese <sup>c</sup>	-2.02	2.4	.402	-0.71	1.6	.656	-4.71	5.9	.429	-1.41	1.3	.278
Linear Age <sub>80/83</sub> <sup>d</sup>	Normal (Ref)	<b>-1.52</b>	<b>0.3</b>	<b>&lt;.001</b>	<b>-0.72</b>	<b>0.2</b>	<b>&lt;.001</b>	<b>-1.71</b>	<b>0.4</b>	<b>&lt;.001</b>	-0.15	0.1	0.166
	Overweight <sup>e</sup>	<b>0.65</b>	<b>0.3</b>	<b>.049</b>	0.06	0.2	.787	0.79	0.6	.196	0.06	0.1	.682
	Obese <sup>e</sup>	<b>1.10</b>	<b>0.5</b>	<b>.027</b>	0.56	0.3	.110	1.15	1.1	.231	0.17	0.2	.407
Baseline Age		2.10	1.2	.070	-0.24	0.7	.729	0.12	1.3	.924	-0.31	0.3	.279

# Women

Intercept <sub>80/83</sub> <sup>b</sup>	Normal (Ref)	<b>57.6</b>	<b>1.4</b>	<b>&lt;.001</b>	<b>29.3</b>	<b>0.9</b>	<b>&lt;.001</b>	<b>44.3</b>	<b>3.0</b>	<b>&lt;.001</b>	<b>10.2</b>	<b>0.7</b>	<b>&lt;.001</b>
	Overweight <sup>c</sup>	1.80	1.4	.200	0.94	0.9	.322	2.64	3.7	.477	0.46	0.9	.599
	Obese <sup>c</sup>	-1.78	1.8	.316	-0.51	1.2	.674	2.95	4.97	.553	-0.94	1.2	.427
Linear Age <sub>80/83</sub> <sup>d</sup>	Normal (Ref)	<b>-0.54</b>	<b>0.2</b>	<b>-.005</b>	<b>-0.417</b>	<b>0.1</b>	<b>.004</b>	-0.72	0.4	.089	-0.11	0.1	.233
	Overweight <sup>e</sup>	0.25	0.3	.360	0.11	0.2	.581	0.06	0.6	.915	0.05	0.1	.739
	Obese <sup>e</sup>	0.04	0.4	.920	0.20	0.3	.486	-0.45	0.8	.593	0.12	0.2	.535
Baseline Age		0.10	1.0	.922	-0.04	0.6	.949	2.097	1.3	.116	0.47	0.3	.140

<sup>a</sup> Controlled for age a baseline.

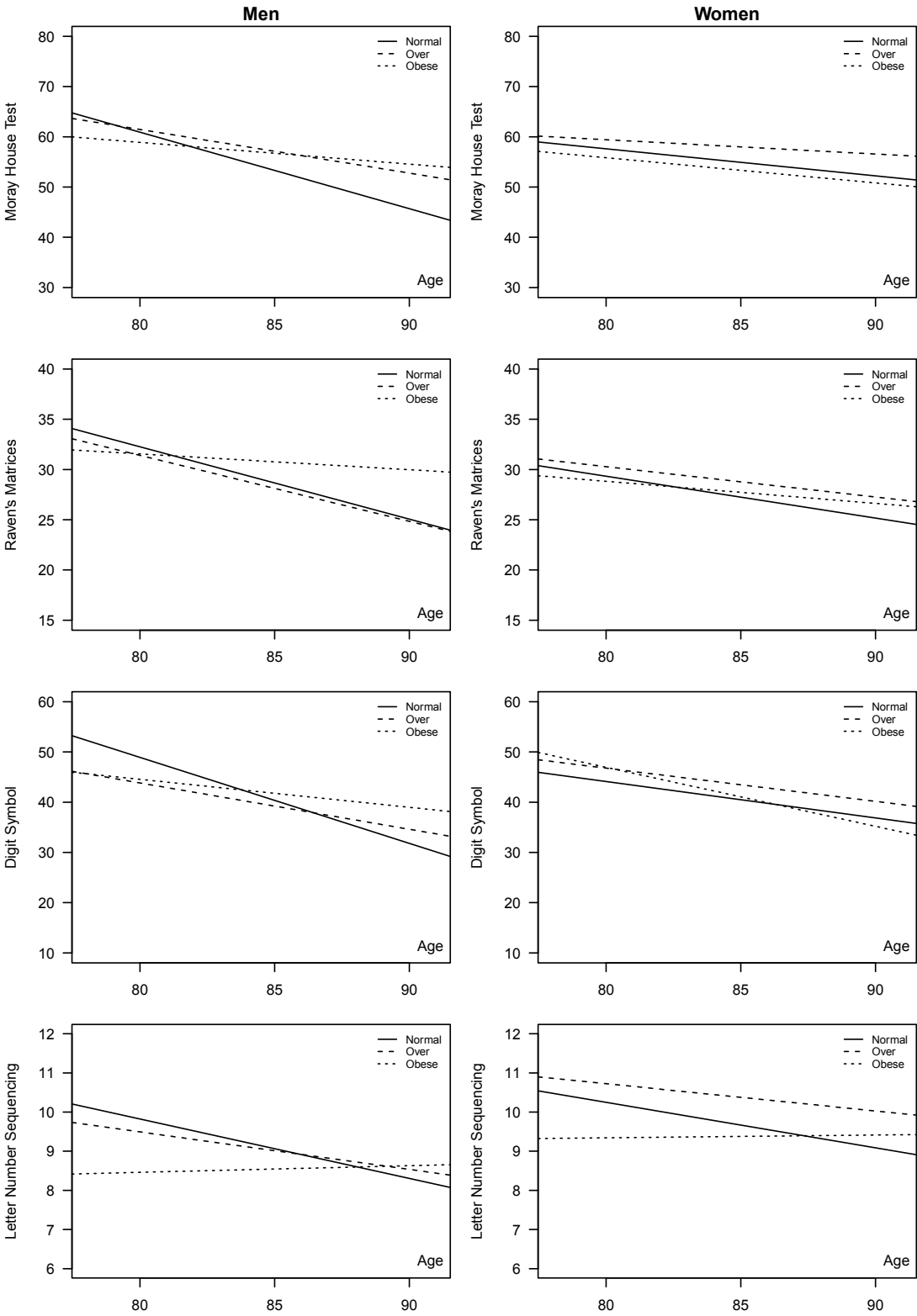
<sup>b</sup> Intercept<sub>80/83</sub>, performance level difference at age 80 for Moray House Test and Raven's Matrices and at age 83 for Digit Symbol and Letter-Number Sequencing due to BMI category.

<sup>c</sup> The estimates represents how much the overweight and the obese persons differ from the normal weight persons at the mean level (the intercept).

<sup>d</sup> Linear Age<sub>80/83</sub>, the rate of which the cognitive function decrease with age.

<sup>e</sup> The estimates represent how much the rate of decline differ for the overweight and obese persons compared to the normal weight persons decline (the linear age).

**Figure 1.** Longitudinal trajectories of cognitive change from age 79 to 90 in the Lothian Birth Cohort 1921.



**Appendix 1.** Cognitive Test Results and Number of Participants at Each Measurement Wave Based on Sex

Wave		Wave 1	Wave 2	Wave 3	Wave 4
<u>Men</u>					
MHT	n	200	-	81	50
	Mean (SD)	60.5 (10.6)	-	53.1 (14.7)	49.7 (15.0)
Raven's Matrices	n	200	128	81	48
	Mean (SD)	32.5 (8.7)	30.9 (9.0)	28.2 (9.8)	25.8 (8.8)
Digit Symbol	n	-	128	79	48
	Mean (SD)	-	42.4 (12.3)	40.6 (12.7)	34.8 (11.9)
Letter-Number	n	-	129	84	53
	Mean (SD)	-	9.7 (2.6)	8.8 (2.8)	9.3 (3.2)
<u>Women</u>					
MHT	n	275	-	97	57
	Mean (SD)	58.3 (10.9)	-	54.9 (12.9)	53.1 (13.9)



Raven's Matrices	n	275	159	97	54
	Mean (SD)	30.1 (8.7)	28.6 (9.3)	27.4 (8.7)	26.4 (8.7)
Digit Symbol	n	-	161	95	53
	Mean (SD)	-	41.1 (13.2)	39.6 (13.1)	35.8 (12.0)
Letter-Number	n	-	161	98	59
	Mean (SD)	-	9.7 (2.9)	9.1 (3.3)	9.3 (3.1)